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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/580,491	05/30/2000	Kurt Hertogs	07691.0009	8312

27777 7590 08/26/2003

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EXAMINER
BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
1631	21

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/580,491	Hertogs et al.
Examiner	**Art Unit**
Michael Borin	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 6/25/03

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 7 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of claims

1. Responses filed 04/01/2003 and 06/25/2003 are acknowledged. Examiner appreciates applicant supplemental response of 06/25/2003 providing response to rejection under 35 U.S.C. 112, first paragraph, and notes that, contrary to applicant's position, the rejection is not a mere re-iteration of previously withdrawn rejection.

Claims 1-30 are pending. Claim 7 is elected, and claims 1-6, 8-30 remain withdrawn from consideration. Cancelation of non-elected claims is requested[1].

Claim Rejections - 35 USC § 102

2. Claim 7 is rejected under 35 U.S.C. 102(b) as anticipated by Condra et al.

The reference evaluates effectiveness of antiviral therapy of HIV patients with protease inhibitor Indinavir (IDV). To evaluate the effectiveness of therapy with IDV, blood of HIV infected patients was collected (same step as step I) of the instant claim), and nucleic acids encoding HIV protease are examined (i.e., as in step (ii)(c) of claim

[1] Upon review of the status of the claims, it was found that due to inadvertent error the previous Office action indicated claim 7 as the only pending claim.

7. In one patient, patient "O" at least one mutation, namely 88T (i.e.,the elected species) correlates with reduced effectiveness of antiviral therapy (see table 1, patient "O") - the resistance to IDV increased to over 3000 nM (see table 1, column IDV CIC and p. 8270, right col., lines 9-10 from bottom). The thus identified at least one mutation correlates with reduced effectiveness of IDV (which reads on step (iii) of the instant claim.

It is the Examiners position that all the elements of Applicant's invention with respect to the method of claim 7 are instantly disclosed by the teaching of the reference cited above.

Response to argument

Applicant argues that it is not possible to pin point drug resistance demonstrated in the reference to just one mutation 88T because the patient displayed a constellation of mutation, 88T being just one of them. Note, however, that the instant claim is drawn to "at least one" mutation, and, therefore, it reads on situations wherein the recited mutation is one of several others.

Applicant further argues that the anticipation rejection is inconsistent with enablement rejection. Examiner respectfully disagrees. These rejections address different embodiments encompassed by the claim: while art rejection addresses situation wherein the claimed mutation is one in a set of others ("at least one"

mutation), the enablement rejection addresses situation when just one mutation is attempted to be used as a marker of drug resistance.

Claim Rejections - 35 USC § 112, first paragraph.

3. Applicants arguments in regard to the enablement rejection are considered and deemed to be persuasive-in-part. The enablement rejection is modified to a scope of enablement rejection as follows.

4. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of evaluating effectiveness of an antiviral therapy by a particular protease inhibitor (nelfinavir) by detecting just one mutation in HIV protease (88T mutation), does not reasonably provide enablement for evaluating effectiveness of the therapy with other antiviral drugs by detecting a single, 88T, mutation in HIV protease.

Claim 7, to the extent it is drawn to the elected species, mutation 88T, is drawn to method of evaluating antiviral therapy of an HIV-infected patient based on identification of mutation 88T in HIV protease. As the claim recites determining "at least one" mutation, the claim encompasses determining only one single 88T mutation; such embodiment is the subject of this rejection.

Prior art teaches that a single residue mutation is not conclusively indicative of development of resistance to HIV therapy. Thus, Condra et al teach that the highly variable nature of the observed amino acid substitutions precludes the identification of simple, invariant rules diagnostic for HIV resistance, no preferred order of appearances of any particular substitution is evident, and that the emergence of phenotypic resistance correlated with the appearance of substitutions at various numbers of amino acid residues among at least 11 sites in HIV protease (rather than just one site as addressed in the instant claim). "No single pattern of amino acid substitution in viral protease was required for the development of resistance to Indinavir. Rather, phenotypic resistance resulted from the combined effects of multiple, highly variable combinations of amino acid variations". See p. 8271, last paragraph; p. 8275, first two paragraphs. Thus, prior art is considered to be unpredictable in regard to correlating a single mutation with resistance to antiviral therapy.

Specification mentions that "mutation at 88T confers resistance to nelfinavir" (p. 25, line 7) [2]. Table I clearly demonstrates that resistance to different antiviral drugs is correlated not with one, but different mutations. Specification does not

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[2] Note, that a different mutation, D30N, is identified elsewhere in the instant specification as the primary mutation in response to nelfinavir. See Table 1, first line.

identify any other drugs for which single 88T mutation is shown to contribute to the drug resistance. Table II informs that 88T mutation is related to resistance to a protease inhibitor (PI); however, no particular PI is identified. The disclosure is not commensurate with the scope of the claimed subject matter. Even though one mutation might contribute to resistance to a drug, detecting just one mutation is not sufficient for successful evaluation of effectiveness of drug therapy. Examiner is not persuaded that detecting a single mutation in HIV protease, such as 88T, would be sufficient to reach objective of the method without undue experimentation.

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

Response to argument

Applicant argues that the description on page 25, as well as data of Table 2 sufficiently demonstrate that mutation 88T confers resistance to nelfinavir. However, as reflected in the revised rejection above, even though the specification is considered enabling in regard to evaluating effectiveness of an antiviral therapy by a particular protease inhibitor, nelfinavir, it does not reasonably provide enablement for evaluating

effectiveness of the therapy with other antiviral drugs by detecting a single mutation at 88T.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are

unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

August 22, 2003

MICHAEL BORIN, PH.D
PRIMARY EXAMINER